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Variable, Not Always Persistent, Postconcussion Symptoms Following Mild TBI in U.S. Military Service Members: A 5-year Cross-sectional Outcome Study

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Abstract

This study examined postconcussion symptom reporting within the first 5 years following mild traumatic brain injury (MTBI). Participants were 167 U.S. military service members (Mean Age = 27.6 years; 74.3% blast; 96.4% male) who were evaluated following injuries sustained in theater during Operations Iraqi and Enduring Freedom (92.8%), or from other combat-related operations. Participants completed the Neurobehavioral Symptom Inventory and PTSD Checklist within three months of injury, and at least one follow-up telephone interview at 6 (*n* = 46), 12 (*n* = 89), 24 (*n* = 54), 36 (*n* = 42), 48 (*n* = 30), and/or 60 months (*n* = 25) post-injury. Approximately half of the sample (49.7%) met DSM-IV symptom criteria for postconcussion disorder (PCD) at baseline. At all six follow-ups, 46.1% to 72.0% met DSM-IV criteria for PCD. However, only 20.4% to 48.0% reported persistent PCD from baseline to follow-up. A substantial minority had also improved (4.0-24.1%) or 'developed' new symptoms (16.9-27.8%). Using regression analyses, baseline symptoms were somewhat predictive of PCD symptom reporting at follow-up, though this was not always reliable. Follow-up for all service members who sustain a combat related MTBI in the context of polytrauma, regardless of the presence/absence of symptom reporting in the acute recovery stage, should be considered the rule, not the exception.

Keywords: mild traumatic brain injury; military service members; postconcussion symptoms

Introduction

Traumatic brain injury (TBI) is common in service members returning from Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF).[1-9] In a study of service members injured in OIF/OEF who were medically evacuated to Walter Reed Army Medical Center, 28% of those injured in combat had sustained a TBI.[10] The Department of Defense (DoD) reported that there were 233,425 brain injuries coded by the DoD Health Care System from 2000 through 2011; 76.6% were mild TBI (MTBI; *n* = 178,961).[11] These data, however, likely underestimate the true prevalence of brain injury in this population because many military personnel with MTBI likely never seek medical treatment or come to the attention of health care providers.

It is expected that the majority of service members who sustain an MTBI in theater will have time-limited symptoms without long-term impairment. Immediately, or within the first 72 hours post-injury, postconcussion symptoms such as slowed reaction time, headache, dizziness, inattention, and impaired judgment are common.[12] However, symptoms tend to resolve to baseline within a month post-injury, with only a small percentage (3-5%) reporting long-term symptoms.[13] Provided there are no further neurological or psychological complications, it is expected that symptoms will not get worse or be cyclical overtime, and new MTBI-related symptoms should not develop in the weeks, months, or years after injury. Of concern however, a large number of service members who incurred a MTBI during deployment to OIF/OEF are reporting symptoms associated with Postconcussion Disorder (PCD) many months or even years post-injury, far in excess of normal recovery times (i.e., 1-3 months). [14, 15]

To date, there are many studies that examine PCD symptom reporting following MTBI at a single time post-injury. However, only few studies have examined the longitudinal course of PCD symptom reporting following MTBI. In a recent civilian study, Meares at al. [16] examined PCD symptom reporting at 2 weeks and 3 months post-injury in 62 uncomplicated MTBI and 58 trauma controls. Almost half of the MTBI group met ICD-10 criteria for PCD at 2 weeks (40.3%) and 3 months (46.8%). However, only 25.8% had PCD at both evaluations; 21% “developed” PCD-like symptoms at follow-up, 14.5% had

"recovered", and 38.7% did not meet criteria at both evaluations. High rates of a PCD-like symptom complex, and a similar pattern of results, were also found in the trauma control group (PCD rates: 2 weeks [50%] and 3 months [48.3%] post-injury. Time 1 versus time 2: Persistent PCD [32.8%], 'developed' PCD [15.5%], 'recovered' [17.2%], no PCD [34.5%]).

In an earlier study, Roe and colleagues [17] examined PCD symptom reporting at 3, 6, and 12 months post-injury in 52 MTBI patients. At 3 months post-injury, 55.8% met ICD-10 criteria for PCD. At 6 and 12 months post-injury, there was a slight decrease in the number of participants who met criteria for PCD (42.3% both times) compared to 3 months post-injury. From 6 to 12 months post-injury, a small percentage of participants 'recovered' (3.8%) and 'developed' PCD (3.8%). From 3 to 12 months post-injury, there was variability in the endorsement of the individual symptoms. A substantial minority of the sample endorsed symptoms that improved (4-25%) or worsened (6-23%) over time.

In one of the largest studies to date, Dikmen and colleagues [18] examined PCD symptom reporting at 1 month and 12 months post-injury in 732 TBI (mixed severity; 63% MTBI) and 120 trauma control patients. At 1 month post-injury, 74% of the TBI group, and 53% of the trauma control group reported three or more symptoms. At 12 months post-injury, there was a slight decline in symptom reporting in both groups; 53% of the TBI group, and 24% of the trauma control group reported three or more symptoms. However, the decline in symptom reporting was not characterized by a uniform improvement from baseline to follow-up. When examining individual symptoms, between 4% to 18% of TBI patients, and 4% to 15% of the trauma control patients reported 'new' symptoms at 12 months post-injury. Irritability and memory problems were most frequently endorsed by both groups.

In the only military study to date, Terrio and colleagues [19] examined symptom ratings at the time of injury (retrospective ratings) and on return from deployment to Iraq in 907 service members with self-reported TBI and 385 injured service members without TBI. Based on a brief five item checklist (headaches, dizziness, memory problems, balance problems, and irritability), 33.4% of the TBI group and 2.9% of the trauma control group endorsed three or more symptoms at the time of injury. On return from

deployment, 7.5% of the TBI group and 2.3% of the trauma control group endorsed three or more symptoms (time since injury was unknown but was less than 12 months). Using three or more symptoms as criteria for PCD, only 5.3% met criteria for PCD at both evaluations; 2.2% "developed" PCD over time, 28.1% had "recovered", and 64.4% did not meet criteria on both occasions (Note: these data are not reported by Terrio and colleagues. Percentages were calculated based on data in the manuscript).

The purpose of this study was to expand on previous work by examining the prospective course of PCD symptom reporting within the first five years following MTBI in service members injured in combat theater. It was hypothesized that PCD symptom reporting in the acute phase of recovery would not be associated with PCD reporting in the chronic phase of recovery.

Materials and Methods

Participants

Participants were 167 U.S. military service members who had sustained a mild TBI and were prospectively recruited from the Walter Reed Army Medical Center (WRAMC; Washington, DC) following injuries sustained in combat theater during OEF/OIF or other combat-related operations, or from other non-combat related incidents. Patients were identified for potential inclusion in the study via regular reviews of all inpatient and outpatient hospital admissions. Patients were targeted for recruitment and consent if they were admitted to WRAMC as a result of physical injuries sustained during combat or non-combat incidents. Patients were enrolled in a larger study if (a) they had been screened positive for TBI as determined by hospital medical staff during a TBI clinical evaluation, (b) they were aged 18 and over, and (c) they had a Rancho Los Amigos level of 7 or higher. General exclusion criteria included the following: (a) the patient or family member was unable to provide surrogate informed consent (i.e. Rancho Los Amigos level less than 7), (b) they had a history of other focal acquired brain injury (i.e. brain tumor or stroke), or (c) they had a history of a psychiatric or neurological disorder. Participants were not excluded if they had a history of prior concussions/TBIs. This information was not available.

Current study participants were selected from the larger group of patients who had sustained a mild, moderate, or severe TBI that had undertaken a TBI clinical evaluation at WRAMC within the first three months of injury (n=369; mild [n=275], moderate [n=81], severe [n=34]). All patients in the larger TBI group had consented to the study and agreed to the use of their clinical data as a baseline evaluation for research purposes. In addition, all patients consented and agreed to participate in annual follow-up evaluations for up to 10 years following enrollment. Participants in the final sample were included if they had sustained a mild TBI (n=275) and they had participated in at least one follow-up evaluation (n=167, 39.3% attrition).

The majority of the participants in the final sample were male (96.4%), had sustained a blast-related injury (74.3%), and had been injured while deployed to OEF/OIF (92.8%). All participants had sustained multiple bodily injuries. Patients typically were medically evacuated from OEF/OIF for limb loss or systemic injuries, rather than mild TBI per se. The mean age of the sample was 27.6 years (*SD* = 7.0). The majority of the sample had experienced less than one minute loss of consciousness (65.3%), less than 15 minutes post-traumatic amnesia (74.9%), and sustained the injury during the first (59.4%) or second (18.0%) deployment.

Clinical Evaluation and TBI Classification

Diagnosis of TBI was based on a routine comprehensive clinical screening evaluation undertaken by medical/health-care professionals at WRAMC. As part of the standard clinical pathway, all patients treated at WRAMC who are considered to be "at risk" for TBI undertake a TBI evaluation. A low threshold is purposely used to classify patients "at risk" for TBI. Typically, patients are considered "at risk" for TBI if they sustained an injury to any part of their body above the shoulders during a battle or non-battle related event, or are injured in any way by an event such as a blast, assault, MVA, or fall. For the large majority of patients, these evaluations are completed by a Physician's Assistant who is trained to evaluate the presence and severity of TBI. In some cases, evaluations are also completed by other health-care professionals such as Neuropsychologists, Social Workers, and Nurses who have specialty training to

evaluate TBI. TBI evaluations typically include (a) a patient interview, (b) a comprehensive medical chart review [including the review of in-theater medical records when available], (c) case conferencing with a multidisciplinary staff, and (d) family interview and gathering of other collateral information [if available]. Subjective patient report is gathered as part of this evaluation but is not relied on for diagnostic purposes. Diagnosis of TBI is based on the presence and duration of loss of consciousness (LOC), presence and duration of post-traumatic amnesia (PTA), duration of alteration of consciousness, and neuroradiological scans. Self-reported symptoms are routinely obtained during the TBI evaluation but are not used for diagnostic or classification purposes (i.e., Neurobehavioral Symptom Inventory [NSI][20] and PTSD Checklist-Civilian [PCL-C]).[21]

Classification of TBI severity

Classification of mild TBI was based primarily on duration of LOC and PTA. GCS scores were not available for use. Mild TBI was defined as follows: PTA <24 hours and LOC <15 minutes. It was our preference to apply a cutoff of LOC <30 minutes, consistent with commonly used diagnostic criteria.[22, 23] However, the available information regarding LOC was limited to categorical data that precluded us from differentiating between LOC greater or less than 30 minutes (i.e., LOC <15 minutes and LOC 16-60 minutes). For those patients with LOC/PTA in the mild range, a classification of mild TBI was assigned regardless of the absence or presence of intracranial abnormality. It is acknowledged that this practice is incongruent with the Department of Defense clinical guidelines [24] that recommends classifying any patient with intracranial abnormality as having a "greater than mild injury" (p.16). However, for the purposes of research, our preference is to classify those patients with evidence of intracranial abnormality and LOC/PTA in the mild range as having a "complicated mild TBI" (rather than moderate TBI). The importance of the distinction between complicated and uncomplicated mild TBI has been discussed elsewhere.[25] In this sample, some patients with LOC/PTA in the mild range also had missing CT/MRI scan information (3.0%). For the purposes of this study, patients were classified as sustaining a mild TBI

regardless of CT/MRI scan results (82.0% uncomplicated mild TBI, 15.0% complicated MTBI, 3.0% unclassified mild TBI).

Measures

Baseline measures included the (a) Neurobehavioral Symptom Inventory (NSI),[20] (b) PTSD Checklist-Civilian; (PCL-C), [21] and (c) Abbreviated Injury Scale (AIS). Follow-up measures included the (d) CTF (Clinical Tracking Form) Telephone Follow-up Interview.

The NSI is a 22-item measure designed to evaluate self-reported postconcussion symptoms (e.g., headache, balance problems, nausea, fatigue, sensitivity to noise, irritability, sadness, nervousness, visual problems). The NSI requires the test taker to rate how much they have been disturbed by each symptom in the last two weeks on a 5-point scale as follows: 0=none, 1=mild, 2=moderate, 3=severe, and 4=very severe. A total score is obtained by summing the ratings for the 22 items (range = 0-88). Participants responses on the NSI can also be classified based on DSM-IV [26] Category C symptom research criteria for Postconcussional Disorder (PCD). PCD classification can be determined based on symptoms reported as 'mild or greater' (i.e., 1, 2, 3, or 4) and 'moderate or greater' (i.e., 2, 3, or 4). Responses on the NSI are classified as meeting DSM-IV research criteria for PCD if the respondent (a) endorses three or more of the Category C symptom criteria, and (b) endorses subjective attention and memory complaints (a proxy for criterion B). Note that only six of the eight Category C criteria are addressed by the NSI items. For the purposes of this study, only those symptoms on the NSI that directly overlapped with those elicited at follow-up were used for direct comparison (i.e., headache, dizziness, balance, memory, fatigue, attention, irritability, depression, concentration, sleep, and anxiety).

The PCL-C is a 17-item measure designed to evaluate self-reported PTSD symptoms. The PCL-C was patterned specifically after the DSM-IV criteria to address Category B, C, and D symptom criteria for PTSD. The PCL-C requires the test taker to rate how much they have been bothered by each symptom in the last month on a 5-point Likert scale (1=not at all, 2=a little bit, 3=moderately, 4=quite a bit, 5=extremely). A total score is obtained by summing the ratings for the 17 items (range = 17-85).

Participant's responses on the PCL-C can also be classified based on DSM-IV criteria for PTSD. PTSD classification can be determine based on symptoms reported as 'mild or greater' (i.e., 2, 3, 4, or 5) and 'moderate or greater' (i.e., 3, 4, or 5). Responses on the PCL-C are classified as meeting DSM-IV criteria for PTSD if the respondent endorses (a) one or more of the Criterion B symptoms (questions 1-5), (b) three or more of the Criterion C symptoms (questions 6-12), and (c) two or more of the Criterion D symptoms (questions 13-17).

The Abbreviated Injury Scale [27] is an anatomically-based, consensus-derived, global severity scoring system that classifies injuries to the body categorized into six main regions (i.e., head or neck, face, chest, abdominal or pelvic contents, extremities or pelvic girdle, and external). Injuries are rated on a 6-point ordinal scale that classifies injury severity as minor (1), moderate (2), serious (3), severe (4), critical (5), or maximal (6). The AIS scoring system has been in use since 1971 and has undergone periodic revisions. The most recent update was in 2008 which was the version used for this study. The AIS is traditionally interpreted using the Injury Severity Score (ISS). The ISS is calculated by summing the squares of the highest AIS severity codes in each of the three most severely injured body regions. The ISS ranges from 1 to 75. For the purposes of this study, a modified ISS score was calculated (ISS_{mod}) to include only extracranial injuries. All AIS codes that included intracranial injuries were not included in the calculation of $ISS_{mod.}$ The ISS_{mod}, however, was calculated in the same manner as the ISS score described above. Classification categories were as follows: Minor (ISS_{mod} 1-3), Moderate (ISS_{mod} 4-8), Serious (ISS_{mod} 9-15), Severe ISS_{mod} 16-24), and Critical (ISS_{mod} 25-75).[28]

The CTF Telephone Follow-up Interview is an unpublished, 10-15 minute, semi-structured interview developed specifically for this study. The interview was designed to provide a 'snap-shot' of key outcome variables commonly examined following TBI (e.g., marital and living situation, health status, access to services, alcohol use, and satisfaction with life). As part of the interview, participants are also required to endorse whether they have any problems with 16 symptoms (headaches, dizziness, memory, attention, concentration, limb weakness, balance, ringing in ears, irritability, sleep, intrusive thoughts,

mood lability, fatigue, depression, anxiety, and sensitivity to noise). Each symptom is read aloud to the participant and he/she was required to confirm the presence or absence of the symptom. Severity ratings were not obtained. A total score is obtained by summing the endorsement of the 16 symptoms (range = 0-16). Participant responses can also be used to classify DSM-IV Category C symptom research criteria for PCD (same as used for the NSI). PCD classification's generating using these symptoms are considered to reflect 'mild or greater' symptom endorsement. For the purposes of this study, only those symptoms that directly overlapped with those symptoms elicited at baseline (i.e., NSI) were used for direct comparison (i.e., headache, dizziness, balance, memory, fatigue, attention, irritability, depression, concentration, sleep, and anxiety).

Procedure

All baseline and follow-up data were collected as part of a prospective longitudinal study. Baseline data were collected in partnership with hospital clinical staff. Participants completed a baseline evaluation within 3 months [baseline] of injury (M=20.7 days, SD = 21.4, range=1-92: 1 to 7 days=27.5%, 8 to 14 days=33.5%, 15 to 21 days=10.8%, 22 to 35 days=9.0%, 36 to 49 days=6.0%, and 50 to 92 days=13.2%). Baseline evaluations were undertaken by hospital medical staff as part of a routine clinical evaluation to determine the presence and severity of TBI on admission to WRAMC (i.e., TBI clinical evaluation). At baseline, all participants were administered the NSI and PCL-C. In addition, the AIS was completed by a physician's assistant within 1-2 months of the evaluation based on a comprehensive medical chart review.

Participants agreed to participate in a 6-month follow-up, followed by annual telephone evaluations for up to 10 years. Follow-up evaluations were undertaken for research purposes only. Participants completed follow-up evaluations by phone at home or in another agreeable location nominated by the participant. For each follow-up evaluation, an attempt was made to contact each participant by phone based on the contact information provided from the previous assessment (baseline or follow-up). On many occasions, contact was unable to be made with the large majority of participants as a

consequence of (a) a change in the participants contact information, or (b) a lack of research personnel available to conduct follow-up phone calls[F1]. For the first 3-4 years of the study, annual follow-up evaluations were conducted on dates that were targeted towards the date of consent (i.e., consent date+12 months [±1 month], consent date+24 months [±1 month], etc.). In an effort to maximize the homogeneity of patients who had completed follow-up evaluations clustered around the anniversary date of their injury, the methodology was modified in 2011 and all annual follow-ups were targeted for completion around the date of injury (i.e., injury date+12 months [±1 month], injury date+24 months [±1 month], etc.).

Participants were classified into follow-up groups based on the number of months that had elapsed since their date of injury and the date of the follow-up evaluation. It was our preference to define follow-up groups based on highly homogenous time periods that clustered around their injury date (e.g., 12 months post-injury [±2 weeks], 24 months post-injury [±1 month], 36 months post-injury [±1 month], etc.). However, due to the early methodological shortcomings of the study (i.e., follow-ups were initially focused on date of consent), this was not possible. Rather, we defined follow-up groups based on a broader range of time that had elapsed between date of injury and the follow-up evaluations. The follow-up groups, and sample sizes in each group, were as follows: (a) 6 months post-injury [6 to <10 months, n=46], (b) 12 months post-injury [10 to <18 months, n=89], (c) 24 months post-injury [18 to <30 months, n=54], (d) 36 months post-injury [30 to <42 months, n=42], (e) 48 months post-injury [42 to <54 months, n=30], (f) 60 months post-injury [54 to <66 months, n=21], and (g) 72 months post-injury [66 to <78 months, n=4]. Due to the small sample sizes in the 60 and 72 month follow-up groups, these two groups were combined to form one group (60+ months post-injury, n=25).

The follow-up groups were not mutually exclusive. Many participants completed a follow-up telephone evaluation at two or more follow-up periods. However, few participants consistently completed two or more follow-up evaluations at the same time periods. The most frequently completed combination of follow-up evaluations was 6/12 months (n=25), followed by 12/48 months (n=19), 12/24 months

[F1] This is an ongoing study. Additional resources were allocated in 2011 to allow for more routine follow-up phone calls to be made.

(n=18), 6/36 months (n=16), 12/36 months (n=15), 12/60 months (n=14), 24/36 months (n=14), 6/24 months (n=12), 24/60 months (n=11), 6/48 months (n=9), 24/48 months (n=9), 36/48 months (n=7), 48/60 months (n=7), 6/60 months (n=6), and 36/60 months (n=5) post-injury.

The protocols under which these data were collected were approved by the Institutional Review Board of WRAMC, Washington, DC. This study was completed in accordance with the guidelines of the Declaration of Helsinki.

Results

Demographic and Injury Characteristics

Demographic and injury characteristics by follow-up group are presented in Table 1 and 2. For the continuous variables (Table 1), across groups, there were no significant main effects for age (p = .802), days tested post injury at baseline (p = .643), baseline NSI total score (p = .675), baseline PCL-C total score (p = .517), or the number of prior blast exposures where the participant was injured or 'knocked down' (p=.581). There were significant main effects for the number of symptoms endorsed at follow-up (p = .008) and bodily injury severity (p = .015). Pairwise comparisons between the six groups revealed few differences however. For the number of symptoms endorsed at follow-up, the only difference was found when comparing the 12-month and 60-month post-injury groups ($p<.05$) with higher levels of symptoms reported at 60-months. Similarly, for bodily injury severity, the only difference was found when comparing the 48-month and 60-month post-injury groups ($p<.05$), again with higher levels at 60-months. As expected, there was a significant main effect for months tested post-injury at follow-up ($p < .001$), however, these differences are due to sample selection only.

For the categorical variables (Table 2), formal statistical comparisons (e.g., chi-square statistics and Fisher exact tests) across all six follow-up groups was not possible due to the large number of groups, multiple categories, and small sample sizes in some cells. However, selected pairwise comparisons were undertaken on those groups with large percent differences. There were no statistical differences for all selected pairwise comparisons (p >.05). No differences were found for gender, duration of LOC and PTA,

mechanism of injury, number of deployments, presence of skull fractures or intracranial abnormality, or amputations.

Symptom Reporting at Baseline and Follow-up

The percentages of the sample meeting DSM-IV criteria for PCD and PTSD at baseline (for the total sample and for each follow-up group), and DMS-IV PCD criteria at follow-up are presented in Table 3. For PCD, approximately half of the total sample met DSM-IV criteria for PCD at baseline (49.7%) based on symptoms endorsed as mild or higher on the NSI, and 25.1% based on symptoms endorsed as moderate or higher. When comparing symptom endorsement on the NSI at baseline across the six groups separately, there were no significant differences in the rates of baseline PCD classification when using symptoms endorsed as mild or higher (p = .643; range = 44.4% to 61.9%) or moderate or higher (p = .238; range = 20.0% to 40.5%).

Similar rates of PCD based on symptoms endorsed as mild or higher were also found at all six follow-up periods (range = 46.1% to 66.7%), with no differences found between groups (p = .056). Comparison of the rates of PCD at follow-up with the rates of PCD at baseline within each group separately (e.g., 24 months post-injury: Baseline PCD=44.4%; Follow-up PCD=48.1%) revealed no significant differences for all groups (all p>.05). Although not statistically significant, it is worth noting that for the 60 months post-injury group, there was a 20% *increase* in the number of those meeting PCD criteria from baseline (52.0%) to follow-up (72.0%).

For PTSD, approximately one quarter of the total sample met criteria at baseline (26.2%) based on symptoms endorsed as "mild or higher" on the PCL-C, and 13.4% based on symptoms endorsed as "moderate or higher". When comparing symptom endorsement on the PCL-C at baseline across the six groups separately, there were no significant differences in the rates of baseline PTSD classification when using symptoms endorsed as mild or higher (p = .887; range = 23.0% to 33.3%) or moderate or higher (p = .815; range = 11.3% to 19.0%).

PCD Symptom Trajectory: Baseline to Follow-up

In order to compare the prospective course of PCD reporting from baseline to follow-up, the number of participants whose symptoms (a) 'improved' [PCD Present-Absent], (b) 'developed' [PCD Absent-Present], (c) 'persisted' [PCD Present-Present], or were (d) 'not present' (PCD Absent-Absent) from baseline to follow-up is presented in Table 4. Overall, there was much variability, and no consistent pattern, in the proportion of each follow-up group that was classified into one of the four "PCD trajectory" categories. Overall, 20.4% to 48.0% of the sample reported 'persistent' PCD symptoms at baseline and at one of the follow-up cohorts. The highest rates of persistent PCD were at 60-months (48.0%) and 36 months (45.2%) post-injury. A substantial proportion of the sample reported an 'improvement' in PCD symptoms from baseline to follow-up (4.0% to 24.1%), or reported 'no PCD' symptoms at both baseline and follow-up (16.7% to 36.0%). The highest rate of no PCD symptoms at baseline and follow-up was at 12 months (36.0%) and 6 months (28.3%) post-injury. The highest rate of improved PCD symptoms at follow-up was at 24 (24.1%) and 12 months (18.0%) post-injury. Of particular interest, 16.9% to 27.8% of the sample reported the 'development' of new PCD symptoms at one of the follow-up periods despite the absence of symptoms at baseline. The highest rate of newly developed PCD symptoms at follow-up was at 24 (27.8%) and 48 months (26.7%) post-injury.

Comparison of Individual PCD Symptoms

In order to compare individual PCD symptom reporting from baseline to follow-up, the number of participants whose individual symptoms (a) 'developed', (b) 'worsened', (c) 'persisted', or (d) was 'not present' from baseline to follow-up was calculated (data not shown; a table can be obtained from RTL on request). The symptoms most commonly reported as 'persisting' over time (i.e., symptom endorsed at baseline and follow-up) in the majority of the six groups, were headaches (41.6% to 68.0%), memory problems (35.2% to 54.8%), irritability (33.3% to 51.9%), and poor sleep (43.8% to 59.5%). However, three of these symptoms (headaches: 23.8% to 40.7%; memory problems: 21.4% to 40.7%; and poor concentration: 19.1% to 33.3%) also were most commonly reported as newly 'developed' over the six follow-up periods (i.e., symptom endorsed at follow-up but not at baseline). In contrast, the symptoms

most commonly reported as 'improving' over time (i.e., symptom endorsed at baseline but not at follow-up) in the majority of the six groups, were dizziness (12.0% to 28.1%) and depression (8.0% to 26.2%). Similarly, the symptoms most commonly reported as 'not present' at baseline and follow-up in the majority of the six groups were dizziness (28.0% to 39.1%), balance problems (28.0% to 50.0%), depression (16.0% to 43.8%) and anxiety (24.0% to 37.1%).

Prediction of Follow-up PCD from All Baseline Symptoms

To examine the influence of symptom reporting at baseline on long-term PCD symptom reporting, a series of *exploratory* regression analyses was undertaken to determine if follow-up PCD status (present versus absent) could be predicted by symptom reporting on the NSI and PCL-C at baseline (mild or higher symptom endorsement). Four predictor variables were examined separately: (a) baseline PCD diagnosis, (b) baseline PTSD diagnosis, (c) the number of NSI symptoms endorsed at baseline, and (d) the number of PCL-C endorsed symptoms at baseline. Four regression analyses were undertaken for each of the six cohorts separately. A summary of the results (p and R^2 values) from the series of regression analyses, and odds ratios (where applicable), is also presented in Table 5 (top half of table = 'All Symptoms').

PCD diagnosis at baseline was a significant predictor of PCD status at 12 months post-injury (p = .004, R^2 = .090, OR = 3.47) and 60 months post-injury (p = .018, R^2 = .222, OR = 12.0), but not for 6, 24, 36, or 48 months post-injury. PTSD diagnosis at baseline was a significant predictor of PCD status only for the 36 months post-injury period (p = .010, R^2 = .154, OR = 11.27). The number of NSI symptoms endorsed at baseline was a significant predictor of PCD status at 6, 12, 36, and 48 months post-injury (all $p < .024$; R^2 =.108 to R^2 =.247), but not at 24 or 60 months post-injury. The number of PCL-C symptoms endorsed at baseline was a significant predictor of PCD status only at 36 and 48 months post-injury (both $p < .012$; R^2 = .225 and R^2 = .206 respectively).

Prediction of Follow-up PCD from Individual Baseline Symptoms

A further series of *exploratory* regression analyses were undertaken to determine if follow-up PCD status (present/absent) could be predicted by the most frequently endorsed symptoms at baseline (mild or higher): sleep problems (65.3%), irritability (60.5%), difficulty concentrating (53.3%), fatigue (52.1%), headaches (50.9%), dizziness (49.1%), and forgetfulness (49.1%). A total of six regression analyses were undertaken for each of the six groups separately by using (a) all seven selected individual symptoms entered simultaneously (regression 1), and (b) the endorsement of either ≥2, ≥3, ≥4, ≥5, or ≥6 of any of the seven symptoms at baseline (regression 2-6). A summary of the results (*p and* R^2 values) from the series of regression analyses, and odds ratios (where applicable), is presented in Table 6 (bottom half of table – 'Individual Symptoms').

Overall, the seven most frequent symptoms reported at baseline were significant predictors of PCD status at 6, 12, 36, and 48 months post-injury ($p < .029$; R^2 =.104 to R^2 =.195), but not 24 and 60 months post-injury. When considering all six symptoms simultaneously, the endorsement of multiple symptoms was a significant predictor of PCD status for all follow-up groups, with the exception of 24 months post-injury. For the 12 and 36 month groups, the use of all multiple symptom combinations (i.e., ≥2, ≥3, ≥4, ≥5, and ≥6) were significant predictors of PCD status at follow-up (all $p <.020$; R^2 =.062 to R^2 =.192; OR=3.67 to OR=8.33). For the 6, 48, and 60 month groups however, only a handful of multiple symptom combinations were significant predictors of PCD status at follow-up (e.g., 6 month post-injury: ≥2 and ≥6 [both $p <.039$], but not ≥3, ≥4, and ≥5 [all $p >.074$]).

PCD Symptom Trajectory: Baseline, Time 1, and Time 2

An attempt was made to compare PCD symptom reporting in a longitudinal manner from baseline to two or more follow-up evaluation periods (i.e., Baseline [Time 1], Time 2, Time 3). Because only a small handful of people had consistently completed two of the same follow-up evaluations (maximum n=25; see Procedure for further details), some follow-up groups were combined in order to increase the sample size of a subgroup that could be compared from baseline across two follow-up periods. Two broad follow-up categories were created: (a) 6/12 months post-injury (range: 6-17 months), and (b) 36/48/60

months post-injury (range: 30-72 months). The 24 month post-injury group was not included in order to create two distinct follow-up categories that were separated by a minimum of 12 months. A total of 50 participants were identified that had completed a follow-up evaluation at 6/12 months and 36/48/60 months. For the 6/12 month follow-up group, if a participant had completed both evaluations (n=4), preference for selection was given to the follow-up evaluation completed at 12 months. In the 36/48/60 month follow-up group, 42% had completed the 48 month evaluation, 40% completed the 26 month evaluation, and 18% had completed the 60 month evaluation. In the event that a person had completed more than one evaluations in this category (n=8), preference for selection was given to the evaluation completed at 48 months, followed by 36 months.

In order to compare the prospective course of PCD reporting from baseline (time 1) to 6/12 months post-injury (time 2) to 36/48/60 months post-injury (time 3), each participants DSM-IV PCD classification was individually examined across the three time periods. Six common PCD trajectories emerged (see Table 6). The most common PCD trajectory was characterized as 'persistent', with 32% of the sample endorsing symptoms consistent with PCD at time 1, time 2, and time 3 (T1-present, T2-present, T3-present). A large minority of the sample (22%) did not endorse symptoms consistent with PCD at all 3 evaluations (T1-absent, T2-absent, T3-absent). Similarly, a large minority (22%) of the sample endorsed PCD symptoms characterized by the 'development and persistence' of PCD symptom reporting over time (T1-absent, T2-present, T3-present). The remaining sample was characterized by 'improvement' of PCD symptoms over time (12%; T1-present, T2-absent, T3-absent), 'late onset' PCD symptoms (6%; T1-absent, T2-absent, T3-present), or 'fluctuating' PCD symptoms (6%; T1-present, T2-absent, T3-present).

Discussion

This study examined the prospective course of PCD symptom reporting within the first 5 years following mild TBI, in US military service members injured while deployed during OEF/OIF and other combat-related operations. It was hypothesized that PCD symptom reporting in the acute recovery phase from mild TBI would be poorly associated with PCD reporting in the chronic recovery phase. Overall,

these results largely support this hypothesis. Approximately half of the service members reported symptoms consistent with DMS-IV criteria for PCD at three months post-injury, and also at 6, 12, 24, 36, 48, and 60+ months post-injury. However, PCD symptom reporting was not characterized by persistent symptom reporting over time, but rather characterized by the persistence (20-48%), improvement (4-24%), or development (19-28%) of PCD symptoms from baseline to one of the six follow-up evaluations. When comparing PCD symptom reporting from baseline to two or more follow-up evaluations in a subset of the sample, PCD symptom reporting was further characterized by the persistence (32%), late development and persistence (22%), improvement (12%), late onset (6%), or fluctuation (6%) of PCD symptoms.

The variability of symptom reporting from baseline to all follow-up periods is further highlighted by our unsuccessful attempts to identify patterns of symptom reporting at baseline that could serve as predictors of chronic symptom reporting. Although there were a handful of measures at baseline that were predictive of PCD status at *some* of the follow-up periods, there was a lack of consistency and reliability in the predictors of long term symptom reporting at follow-up to be considered useful markers of poor outcome. At best, (a) the number of symptoms reported at baseline, or (b) the frequency of commonly reported symptoms at baseline (i.e., sleep, irritability, fatigue, dizziness, headaches, and concentration) were the best predictors of follow-up symptoms. However, these variables explained only a small amount of variance and were not consistent across all six follow-up periods.

The variability of PCD symptom trajectories in this sample is consistent with other studies.[16-18] Meares and colleagues [16] reported similar PCD rates at 2 weeks (40.3%) and 3 months (46.8%) following MTBI. However, only 25.8% actually had persistent PCD from baseline to follow-up; 21% "developed" new PCD symptoms, and 14.5% had "recovered". Remarkably, almost identical results were also found in a group of patients who had sustained orthopedic injuries without TBI. Similarly, Dikmen and colleagues [18] reported high rates of PCD symptom reporting at 1 month and 12 months post-injury following TBI and orthopedic injury. Despite a small decrease in symptom reporting from baseline to follow-up in both groups (TBI: 74% to 53%; Trauma Control: 53% to 24%), symptom endorsement was variable. Between

4-18% of TBI patients, and 4-15% of the trauma control patients reported 'new' symptoms at 12 months post-injury, but not at 1 month post-injury. Somewhat inconsistent with the above, Roe and colleagues [17] found little variation in overall PCD classification at 3, 6, and 12 months post-injury. The majority of people who met PCD criteria at 6 and 12 months remained relatively stable. Only 3.8% of the sample "recovered" and 3.8% "developed" new PCD symptoms. However, there was much variability in individual symptom reporting from 3 to 12 months. A substantial minority of the sample endorsed symptoms that had improved (range: 4-25%) or worsened (range: 6-23%) over time.

The 'development' of PCD-like symptoms long after a remote mild TBI is likely due to many factors unrelated to the brain injury itself. It is important to appreciate that many non-TBI factors can cause, maintain, or mimic self-reported PCD symptoms (e.g., comorbidities, social-psychological factors, or legal factors). [2, 5, 15, 29, 30, 31] PCD symptoms are not unique to mild TBI alone and these symptoms often overlap with a number of pre-existing and/or co-occurring conditions, or are simply symptoms that were present prior to the injury. Researchers have repeatedly demonstrated that healthy adults without brain injury report very similar symptoms [32-40] as do various non-mild TBI clinical groups such as those with psychiatric disorders, personal injury claimants, and those with chronic pain, PTSD, and soft-tissue injuries. [41-51] Complicating matters further, the perception and reporting of symptoms long after a mild TBI can be influenced by premorbid personality characteristics,[31, 52-55] depression,[56] and a diverse range of social-psychological factors (e.g., expectations, misattribution, and an idealized view of pre-injury functioning.[35, 57-64] The interested reader is directed to Iverson and colleagues [65] for a more comprehensive discussion of these issues.

PCD symptom reporting following mild TBI in a military setting is especially complicated and is often confounded by exposure to emotionally traumatic events and comorbid physical injuries[66]. PCD symptoms have been endorsed by military personnel following episodes of in-theater distressing experiences, even with no causal link to a TBI-producing event (i.e., aiding the wounded).[12] Even in the absence of brain injury, polytrauma patients endorse high rates of psychological and neurobehavioral

symptoms, including memory problems, significant mood symptoms, and amotivation. [67] Among returning service members with mild TBI, high levels of mental health comorbidity are commonly cited, [14, 68-70] making it difficult to tease out other potential causes for PCD-like symptoms, such as PTSD and depression.[66] High rates of depression, PTSD, and substance abuse have also been reported, especially in those service members exposed to, or wounded in combat.[66, 71-74] Mental health problems can manifest at varying time points and tend to intensify with time.[75-80] In a sample of service members returning from Iraq, less mental health distress was reported immediately upon return than at 4-10 months post-return.[79] Interestingly, in our sample, we noted a slight increase in PCD symptom reporting from 12 months (44.3%) to 36 months (61.3%) and 48 months (63.6%) post-injury. It is possible that this slight increase in PCD symptom reporting is due to (a) the presence of other clinical conditions that have similar, non-specific symptoms (e.g., PTSD, depression, sleep disorders, chronic pain), or (b) simply reflects a sample selection bias towards the participation of those service members who are symptomatic at the time of evaluation.

In partial support for the influence of PTSD on PCD symptom reporting in the chronic phase of recovery in this sample, the number of PCL-C symptoms at baseline was somewhat predictive of PCD diagnosis at 36 and 48 months post-injury, but not at 8, 12, 18, or 24 months post-injury. Past studies have found that PTSD and depression largely explain the relationship between a history of mild TBI and persistent PCS reporting, along with other general health/psychosocial symptoms.[14, 70, 81, 82] Cooper and colleagues [83] found that mild TBI participants with high levels of PTSD reported significantly more PCD than those reporting low levels of PTSD. Brenner and colleagues[84] found that mild TBI alone or PTSD alone were associated with a higher prevalence of PCD than those with neither diagnosis. A diagnosis of both mild TBI and PTSD was more strongly associated with PCS than either mild TBI alone or PTSD alone. The findings are also consistent with the civilian literature.[16] Of course, it is possible that the relation between PCD and PTSD symptom reporting may be simply due to the presence of a number of overlapping symptoms that are commonly reported following MTBI and PTSD (e.g., poor concentration,

irritability, depression, sleep problems, anxiety). Differentiating between the contribution of brain injury and/or PTSD on symptom reporting following deployment is complicated. It is important to note however, that in contrast to past research, the relation between PTSD and PCS in this sample was (a) only found 3 or more years post-injury, and (b) the association was considered weak, with less than 23% of the variance accounted for by PTSD in the prediction of PCD.

The current study has several methodological limitations. First, the attrition rate in this sample was very high. From a total of 275 participants with mild TBI recruited for the study, only 167 completed one or more follow-up evaluations. This reflects a 39.3% attrition rate overall from baseline to any follow-up. However, the rate of attrition is actually much higher when you consider the each annual follow-up evaluation separately [i.e., 6 month follow-up (83.3%), 12 month follow-up (67.6%), 24 month follow-up (80.1%), 36 month follow-up (81.3%), 48 month follow-up (82.5%), 60+ month follow-up (80.6%)][F2]. The high attrition rates at all follow-up evaluations were largely due to a lack of research personnel available to conduct follow-up phone calls within the first 2-3 years of the study. As such, the attrition rates are considered to reflect benign random attrition caused by administrative factors, rather than reflecting a bias in sampling as a result of participants declining, or who are willing, to participate. The sample in this study is considered much more representative of the larger mild TBI population than is indicated by these high attrition rates. Second, the accurate identification of mild TBI in combat-injured polytrauma cases is complex. It is possible that we have included a small number of patients who did not sustain an obvious mild TBI and a few who might have sustained a more serious injury. Further research into the accurate diagnosis of mild TBI in a polytrauma population seems needed. Third, information regarding compensation status or external incentives was not available in this sample. Although it is common for service members to have external incentives at the time of testing (e.g., avoiding being deployed again, obtaining a disability pension or other financial incentive), this information was not

[F2] These attrition rates take into account the number of people who were not yet eligible for follow-up evaluations at 6 months (n=0), 12 months (n=0), 24 months (n=3), 36 months (n=50), 48 months (n=104), and 60+ months (n=146) post-injury. Attrition rates were calculated against the larger sample size of n=275 eligible mild TBI participants.

available and we could not evaluate the influence of external incentives on symptom reporting. Fourth, severity ratings of the symptoms at follow-up were not obtained. Symptoms at follow-up were simply endorsed as "present" or "absent". As such, the comparison of PCD rates from baseline and follow-up were limited to symptoms that were reported as "mild or higher" (baseline) and "present" (follow-up). The use of these criteria has likely over-estimated PCD rates in this sample. Applying a criterion of "moderate of higher" would have been more suitable. Fifth, for the baseline and follow-up evaluations, no information was gathered with respect to the onset of symptoms (e.g., were the symptoms present prior to the injury?). For all evaluations, the respondent was required to report the absence or presence of symptoms within the past few weeks of the examination. This method of symptom measurement fails to capture some important information regarding onset and duration of symptoms that may be clinically relevant. Finally, it is not possible to determine the role of a symptom exaggeration (or secondary incentives) on these results because this information was not part of the study design or available in the database. Symptom exaggeration is common in military service members following TBI.[85] It is likely that there are a number of participants who have either exaggerated the presence of symptoms, exaggerated the severity of symptoms, or both.

In conclusion, recovery from mild TBI in a military setting is complex and often confounded by exposure to blast, combat, emotionally traumatic events, and physical injury. These factors are routinely experienced by a service member over multiple deployments, making it difficult to differentiate other potential causes for PCD-like symptoms, such as mental health comorbidity, sleep problems, chronic pain, or medication use. These and other contributing factors need to be considered when evaluating symptom reporting following mild TBI in this population. Nonetheless, regardless of the etiology of symptoms reported by service members, it was alarming to see the high prevalence of symptom endorsement consistently across the first four years following injury. Extended follow-up for all service members who sustain a combat-related mild TBI with polytrauma, regardless of the presence/absence of symptom reporting within the first few months post-injury, should be considered.

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Table 1

Demographic and Injury Severity Characteristics by Cohort: Continuous Variables

	6 months post-injury		12 months post-injury		24 months post-injury		36 months post-injury		48 months post-injury		60 months post-injury		
	M (SD)		*M (SD)*		*M (SD)*		*M (SD)*		*M (SD)*		*M (SD)*		*p*[3]
Age (Base)	27.4	7.6	27.0	6.5	28.0	7.8	27.7	7.1	26.5	6.9	25.8	5.6	.802
Days tested post-injury (Base)	16.1	16.2	20.3	21.2	20.2	21.9	23.1	22.0	23.7	26.4	21.9	21.1	.643
NSI total score (Base)	18.9	15.6	16.8	15.4	17.6	14.8	21.7	15.1	17.7	15.8	17.3	15.6	.675
PCL-C total score (Base)	31.4	13.3	29.8	13.1	31.5	12.9	35.0	15.1	32.9	14.3	31.4	15.9	.517
Number of follow-up Sx (All)[1]	8.5	4.2	7.8_a	4.8	9.5	4.4	9.9	4.6	9.2	4.5	11.7_a	3.6	.004
Number of follow-up Sx (PCD)[2]	6.4	3.1	5.7_a	3.6	6.7	3.1	7.1	3.5	6.6	3.3	8.4_a	2.4	.008
AIS-ISS score (Base)	23.3	30.4	30.3	35.9	34.6	37.2	35.2	39.1	15.1_b	18.0	46.4_b	42.0	.015
Number of prior blast exposures[4]	1.2	1.5	1.3	1.3	1.0	0.7	1.0	0.8	1.2	1.2	1.1	0.7	.581

Note: *N* = 167; Sample sizes for follow-up subgroups: 6 months post-injury (*n* = 46), 12 months post-injury (*n* = 89), 24 months post-injury (*n* = 54), 36 months post-injury (*n* = 42), 48 months post-injury (*n* = 30), 60 months post-injury (*n* = 25). Abbreviations: Base = Baseline, FUp = Follow-up, NSI = Neurobehavioral Symptom Inventory, PCL-C = PTSD Checklist-Civilian, PCD = selected Postconcussion Disorder symptoms, AIS-ISS = Abbreviated Injury Scale: modified Injury Severity Score (intracranial injuries were excluded from the calculation of ISS). Footnotes: [1]maximum of 16 symptoms; [2]maximum of 11 symptoms; [3]common subscript = p<.05 for pairwise comparisons. [4]Number of prior blast exposures where the participant was injured or ‘knocked down’.

Table 2
Demographic and Injury Characteristics by Cohort: Categorical Variables

		6 months post-injury	12 months post-injury	24 months post-injury	36 months post-injury	48 months post-injury	60 months post-injury	MIN	MAX	% diff[1]
Gender	Male	95.7	96.6	94.4	92.9	96.7	92.0	92	96.7	4.7
Loss of consciousness	None	21.7	23.6	17.6	28.5	36.6	20.0	17.6	36.6	19.0
	<1 min	39.1	49.4	51.9	45.2	46.7	60.0	39.1	60.0	20.9
	1 to 15 mins	39.1	27.0	29.6	26.2	16.7	20.0	16.7	39.1	22.4
Post-traumatic amnesia	<1 min	43.5	43.8	51.9	50.0	36.7	60.0	36.7	60.0	23.3
	1 to 15 mins	37.0	31.5	29.6	26.2	36.7	16.0	16.0	37.0	21.0
	16 to 59 mins	8.7	15.7	14.8	4.8	10.0	12.0	4.8	15.7	10.9
	1 to 24 hours	10.9	9.0	3.7	19.0	16.7	12.0	3.7	19.0	15.3
Mechanism of injury	Non-Blast	26.1	21.3	25.9	28.6	26.7	24.0	21.3	28.6	7.3
	Blast	73.9	78.8	74.1	71.4	73.3	76.0	71.4	78.8	7.4
Where wounded	OIF	80.4	85.4	79.6	69.0	86.7	84.0	69.0	86.7	17.7
	OEF	13.0	9.0	14.8	23.8	10.0	8.0	8.0	23.8	15.8
	Other GWOT	6.5	5.6	5.6	7.1	3.3	8.0	3.3	8.0	4.7
Deployment number	First	52.2	60.7	64.9	57.2	66.7	60.0	52.2	66.7	14.5
	Second	15.2	14.6	24.1	26.2	10.0	8.0	8.0	26.2	18.2
	Third or more	13.0	12.4	7.5	7.1	10.0	16.0	7.1	16.0	8.9
	Missing/NA	19.6	12.3	3.5	9.5	13.3	16	3.5	19.6	16.1
Amputations	Absent	87.0	91.0	85.2	85.7	96.7	84.0	84.0	96.7	12.7
	Present	13.0	7.9	13.0	11.9	3.3	12.0	3.3	13.0	9.7
	Unknown	--	1.1	1.9	2.4	--	4.0	1.1	4.0	2.9
CNS injuries	Absent	73.9	82.0	83.3	83.3	80.0	68.0	68.0	83.3	15.3
	Present	21.7	13.5	16.7	14.3	20.0	24.0	13.5	24.0	10.5
	Unknown	4.3	4.5	--	2.4	--	8.0	2.4	8.0	5.6
Skull fracture	Absent	87.0	91.0	90.7	88.1	96.7	80.0	80.0	96.7	16.7
	Present	10.9	6.7	9.3	9.5	3.3	12.0	3.3	12.0	8.7
	Unknown	2.2	2.2	--	2.5	--	8.0	2.2	8.0	5.8

Note: $N = 167$; Sample sizes for follow-up subgroups: 6 months post-injury ($n = 46$), 12 months post-injury ($n = 89$), 24 months post-injury ($n = 54$), 36 months post-injury ($n = 42$), 48 months post-injury ($n = 30$), 60 months post-injury ($n = 25$). Abbreviations: BS = Baseline, FU = Follow-up. Footnotes: [1]Statistical comparisons across the six groups were unable to obtained due to the large number of groups and cells; [2]Fisher Exact Tests: $p = .031$

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Table 3

NSI and PCL-C symptom Endorsement at Baseline and Follow-up: Percentage Meeting DSM-IV Criteria for PCD and PTSD by Cohort

	Total sample (Baseline)	6 months post-injury	12 months post-injury	24 months post-injury	36 months post-injury	48 months post-injury	60 months post-injury	MIN	MAX	% diff[1]
DSM-IV PCD Criteria (Baseline)[3]										
Present (≥mild Sx)	49.7	50.0	47.2	44.4	61.9	50.0	52.0	44.4	61.9	17.5
Present (≥moderate Sx)	25.1	26.1	22.5	20.4	40.5	30.0	20.0	20.0	40.5	20.5
DSM-IV PCD Criteria (Follow-up)										
Present (≥mild Sx)	--	54.3	46.1	48.1	66.7	66.7	72.0	46.1	72.0	25.9
DSM-IV PTSD Criteria (Baseline)[2]										
Present (≥mild Sx)	26.2	26.7	23.0	24.5	33.3	26.7	24.0	23.0	33.3	10.3
Present (≥moderate Sx)	13.4	15.6	11.5	11.3	19.0	10.0	16.0	10.0	19.0	9.0

Note: N = 167; Sample sizes for follow-up subgroups: 6 months post-injury (n = 46), 12 months post-injury (n = 89), 24 months post-injury (n = 54), 36 months post-injury (n = 42), 48 months post-injury (n = 30), 60 months post-injury (n = 25). Abbreviations: BS = Baseline, FU = Follow-up. Footnotes: [1]For exploratory purposes only, the Chi-square statistic is reported here. The Fishers Exact test statistic is the appropriate value to report here due to 1 cell with an expected count of 5. However, Fishers Exact test was unable to be obtained here due to the large number of groups and cells; [2]PCD criteria = NSI symptoms: endorsement of (a) three or more of the Category C symptoms, and (b) subjective complaints of attention or memory (Note: Category D criteria requires objective evidence of cognitive impairment in attention or memory. For the purposes of this study, subjective reports of these cognitive complaints were used as a proxy because all the subjects did not undergo neuropsychological testing). [3]PTSD criteria = PCL-C symptoms: endorsement of (a) one or more of the Criterion B symptoms (questions 1-5), (b) three or more of the Criterion C symptoms (questions 6-12), and (c) two or more of the Criterion D symptoms (questions 13-17).

Table 4
Comparison of PCD Status from Baseline to Follow-up by Cohort[1]

	6 months post-injury	12 months post-injury	24 months post-injury	36 months post-injury	48 months post-injury	60 months post-injury	MIN	MAX	% diff[1]
Improved (Present-Absent)	17.4	18.0	24.1	16.7	10.0	4.0	4.0	24.1	20.1
Developed (Absent -Present)	21.7	16.9	27.8	21.4	26.7	24.0	16.9	27.8	10.9
Persistent (Present-Present)	32.6	29.2	20.4	45.2	40.0	48.0	20.4	48.0	27.6
Not Present (Absent-Absent)	28.3	36.0	27.8	16.7	23.3	24.0	16.7	36.0	19.3

Note: $N = 167$; Sample sizes for follow-up subgroups: 6 months post-injury ($n = 46$), 12 months post-injury ($n = 89$), 24 months post-injury ($n = 54$), 36 months post-injury ($n = 42$), 48 months post-injury ($n = 30$), 60 months post-injury ($n = 25$). Abbreviations: BS = Baseline, FU = Follow-up. Footnotes: [1]DSM-IV PCD was defined as follows: (a) 3 or more Category C criteria, and (b) subjective complaints of Poor Memory/Concentration. Note that only 6 of the 8 Category C symptom criteria for PCD can be addressed by the NSI and CTF items. Note that the prevalence of PCD reported using CTF and NSI mild symptoms are directly comparable. [1]Statistical comparisons unable to obtained due to the large number of groups and cells

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Table 5

Summary of Regression Analyses and Odds Ratios: Prediction of Follow-up DSM-IV PCD Status (Present) from Baseline Symptom Reporting

	6 months post-injury			12 months post-injury			24 months post-injury			36 months post-injury			48 months post-injury			60 months post-injury		
Predictor Variable at Baseline	*p*	R^2	*OR*	*p*	R^2	*OR*	*p*	R^2	*OR*	*p*	R^2	*OR*	*p*	R^2	*OR*	*p*	R^2	*OR*
All Symptoms																		
DSM-IV PCD Dx	.145	4.8	2.43	.004	9.0	3.47	.766	0.2	0.85	.272	3.0	2.11	.130	8.0	3.50	.018	22.2	12.0
DSM-IV PTSD Dx	.426	1.4	3.18	.687	0.2	1.23	.671	0.3	0.95	.010	15.4	11.27	.155	7.1	4.85	.499	2.0	2.31
Number of NSI Sx	.008	14.9	--	.002	10.8	--	.424	1.2	--	.001	24.7	--	.024	16.8	--	.093	11.7	--
Number of PCL-C Sx	.089	6.6	--	.116	2.9	--	.495	0.9	--	.002	22.5	--	.012	20.6	--	.060	14.5	--
Individual Symptoms																		
7 Selected Sx*	.029	10.4	--	.001	13.4	--	.483	1.0	--	.003	19.5	--	.017	18.7	--	.152	8.7	
≥2 of any 7 selected Sx	.039	9.3	4.51	.019	6.2	3.60	.845	0.1	1.15	.186	4.3	3.55	.136	7.8	3.78	.890	1.0	0.83
≥3 of any 7 selected Sx	.098	6.1	2.88	.001	11.9	4.86	.207	3.0	2.16	.004	18.9	8.33	.017	18.7	7.00	.751	0.4	1.40
≥4 of any 7 selected Sx	.158	4.5	2.37	.003	9.7	3.67	.403	1.3	1.60	.020	12.8	4.89	.130	8.0	3.50	.092	11.9	5.00
≥5 of any 7 selected Sx	.074	7.1	3.00	.002	10.1	3.83	.635	0.4	1.32	.004	19.2	7.74	.017	18.8	11.0	.033	18.3	5.60
≥6 of any 7 selected Sx	.007	15.6	6.50	.001	15.5	6.15	.887	0.1	1.10	.014	14.2	6.92	.097	9.5	6.00	.055	15.1	4.46

Note: *N* = 167; Sample sizes for follow-up subgroups: 6 months post-injury (*n* = 46), 12 months post-injury (*n* = 89), 24 months post-injury (*n* = 54), 36 months post-injury (*n* = 42), 48 months post-injury (*n* = 30), 60 months post-injury (*n* = 25). Abbreviations: NSI = Neurobehavioral Symptom Inventory, PCL-C = PTSD Checklist-Civilian, PCD=Postconcussion Disorder, PTSD = Post-traumatic Stress Disorder. *7 Selected Symptoms = dizziness, headaches, concentration, memory, fatigue, sleep, irritability.

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Table 6
Comparison of PCD Status from Baseline to Multiple Follow-ups: Subgroup Analysis

	Baseline: <3 months post-injury	Follow-up 1: 6-12 months post-injury	Follow-up 2: 36-60 months post-injury	n	%
No PCD	Absent	Absent	Absent	11	22.0
Very Late Development of PCD	Absent	Absent	Present	3	6.0
Late Development and Persistence of PCD	Absent	Present	Present	11	22.0
Improved PCD	Present	Absent	Absent	6	12.0
Fluctuating PCD	Present	Absent	Present	3	6.0
Persistent PCD	Present	Present	Present	16	32.0

NOTE: n=50; Baseline: range = 3-92 days (<30 days = 84%); Follow-up 1: range = 6-18 months (6-14 months = 78%); Follow-up 2: range = 30-72 months (30-50 months = 80%).